PROCRIT® (epoetin alfa)
Every-Three-Week Dosing in Treating Anemia in Patients with Cancer

SUMMARY

- Initiate PROCRIT in patients on cancer chemotherapy only if the hemoglobin is less than 10 g/dL, and if there is a minimum of two additional months of planned chemotherapy.[1]
- Use the lowest dose of PROCRIT necessary to avoid RBC transfusions.[1]
- In a prospective, open-label, multicenter study evaluating epoetin alfa (EPO) 80,000 Units (U) once every 3 weeks (Q3W); EPO 120,000 U Q3W; EPO 40,000 U once weekly (QW); and darbepoetin alfa (DARB) 500 µg Q3W as initial dosing in patients with chemotherapy (CT)-associated anemia (N=236), there were no significant differences between groups in the proportion of patients who achieved either hemoglobin (Hb) ≥11.5 g/dL or increment of Hb >2.0 g/dL from pretreatment values (61.7%, 65.5%, 68.9%, and 66.7% for the EPO 80,000 U Q3W; EPO 120,000 U Q3; EPO 40,000 U QW; and DARB 500 µg Q3W groups, respectively [*P*<0.41 for all comparisons]). The incidence of grade 3/4 adverse events (AEs) and on-study deaths were similar between groups.[2]
- In a prospective study evaluating EPO 120,000 U Q3W as initial dosing in cancer patients with CT-induced anemia (N=186), 60% of patients in the early and standard intervention groups had weekly Hb values during CT within the Hb target of 11-13 g/dL. Patients who remained on Q3W dosing and were not switched to 40,000 U QW had significant mean increases in Hb (*P*<0.05) from baseline for all groups. Four drug-related AEs, including pain, injection site pain, bone pain, and deep vein thrombosis (DVT), were considered very likely related to study drug. The incidence of ≥1 clinically relevant thrombotic vascular event (CRTVE) was similar in all treatment groups.[3]
- A randomized, multicenter study (N=360) found that EPO 120,000 U Q3W maintenance dosing resulted in comparable transfusion requirements (18% vs 23%; *P*=0.22) compared with maintenance dosing with 40,000 U QW in patients with cancer-associated anemia who were initiated on EPO 40,000 U QW. The incidence of AEs and ischemic/thrombotic events was comparable between groups.[4]
- In a prospective, open-label, single-arm, multicenter study evaluating EPO 80,000 U Q3W maintenance therapy in cancer patients with CT-induced anemia initiated on EPO 60,000 U QW (N=115), 76.4% of patients achieved a Hb increase ≥2 g/dL from baseline or achieved a Hb level ≥12 g/dL. Serious adverse events (SAEs) were reported in 44.3% of patients. CRTVEs were experienced by 7.8% of patients in the initial dosing phase (IDP) and none during the maintenance dosing phase.[5]
- Smaller prospective studies (N≤50) have also investigated the use of EPO Q3W dosing.[6,7] In addition, retrospective analyses of medical claims databases corroborate the findings from the clinical studies described in this summary.[8-18] The claims databases support dosing of EPO beyond QW and show extended dosing to be common for initiation as well as maintenance therapy.

BACKGROUND

Various studies evaluating extended or alternative dosing regimens of EPO have been conducted in cancer patients with anemia receiving myelosuppressive CT as well as in anemic cancer patients not receiving CT or radiation therapy. Extended/alternative dosing regimens of EPO may potentially offer added convenience to both health care providers and the patient.[19]

PRODUCT LABELING

Recommended Starting Dose[1]

Adults:

- 150 Units/kg subcutaneously 3 times per week until completion of a chemotherapy course or
- 40,000 Units subcutaneously weekly until completion of a chemotherapy course.

Pediatric Patients (5 to 18 years):

- 600 Units/kg intravenously weekly until completion of a chemotherapy course.

Dose Reduction[1]

Reduce dose by 25% if:

- Hemoglobin increases greater than 1 g/dL in any 2-week period or
- Hemoglobin reaches a level needed to avoid RBC transfusion.
- Withhold dose if hemoglobin exceeds a level needed to avoid RBC transfusion. Reinitiate at a dose 25% below the previous dose when hemoglobin approaches a level where RBC transfusions may be required.

Dose Increase[1]

- After the initial 4 weeks of PROCRIT therapy, if hemoglobin increases by less than 1 g/dL and remains below 10 g/dL, increase dose to:
  - 300 Units/kg three times per week in adults or
  - 60,000 Units weekly in adults
  - 900 Units/kg (maximum 60,000 Units) weekly in pediatric patients
- After 8 weeks of therapy, if there is no response as measured by hemoglobin levels or if RBC transfusions are still required, discontinue PROCRIT.

CLINICAL STUDIES

Initiation: Q3W Dosing

EPO 80,000 U Q3W or 120,000 U Q3W

Steensma et al (2015)[2] evaluated the efficacy and safety of an initial dose of EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W in patients with CT-associated anemia (N=236).

Study Design/Methods

- This was a prospective, open-label, multicenter study.
- Patients who were receiving or were planning to receive CT for a non-myeloid malignancy, had Hb <10.5 g/dL, serum ferritin >20 ng/mL, weight >40 kg and <150 kg, Eastern Cooperative Oncology Group performance status (ECOG PS) ≥ 2 or better, and no evidence of another cause of anemia (eg, hemolysis, hemorrhage, myelodysplastic syndrome, or iron, folate, or B_{12} deficiency) were randomized 1:1:1:1 to receive either: EPO 80,000 U subcutaneously (SC) Q3W; EPO 120,000 U SC Q3W; EPO 40,000 U SC QW; or DARB 500 µg SC Q3W for 15 weeks.
- EPO and DARB were withheld for Hb >12 g/dL and restarted at a lower dose when Hb fell to ≤11.5 g/dL.
- Dose escalations were not permitted.
- Patients received ferrous sulfate 325 mg orally once daily as tolerated.
- **The primary endpoint** was the proportion of patients achieving a Hb response, either Hb ≥11.5 g/dL or increment Hb >2.0 g/dL from pretreatment values.

Results

Patient Characteristics

- A total of 60 patients received EPO 80,000 U Q3W; 58 patients received EPO 120,000 U Q3W; 61 patients received EPO 40,000 U QW; and 57 patients received DARB 500 µg Q3W.
- A total of 45%, 46.6%, 44.3%, and 43.9% of patients in the EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W groups received platinum-containing regimens, respectively.
- Mean baseline Hb was 9.7 g/dL, 9.7 g/dL, 9.8 g/dL, and 9.7 g/dL in the EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W groups, respectively.
- The number of females per group was 60%, 43%, 39%, and 26% for the EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W groups, respectively ($P<0.05$).

Efficacy

- The proportion of patients who achieved a Hb response was 61.7%, 65.5%, 68.9%, and 66.7% for the EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W groups, respectively ($P<0.41$ for all comparisons).
- The Hb increment from baseline to end-of-study was higher in the EPO 40,000 U QW and DARB 500 µg Q3W groups vs the EPO 80,000 U Q3W and EPO 120,000 U Q3W groups (median EPO 40,000 U QW: 2.8 g/dL, DARB 500 µg Q3W: 2.6 g/dL, EPO 80,000 U Q3W: 2.0 g/dL, EPO 120,000 U Q3W: 2.1 g/dL; $P=0.005$ for comparison of EPO 40,000 U QW vs EPO 80,000 U Q3W; $P=0.01$ for EPO 40,000 U QW vs EPO 120,000 U Q3W; $P<0.05$ for comparisons of DARB 500 µg Q3W vs EPO 80,000 U Q3W and EPO 120,000 U Q3W).
- Hb response was achieved in 50, 49, 32, and 49 days in the EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W groups, respectively.
- The proportion of patients who received red blood cell transfusions was 33.3%, 22.4%, 27.9%, and 29.8% in the EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W groups, respectively.
- The mean total dose of EPO used was 240,000 U; 360,000 U; and 265,000 U in the 80,000 U Q3W; 120,000 U Q3W; and 40,000 U QW groups, respectively ($P=0.0009$ for EPO 40,000 U QW vs EPO 120,000 U Q3W groups).
- The proportions of patients who omitted ≥1 dose due to a high Hb were 30.0%, 34.5%, 63.9%, and 43.6% for the EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W groups, respectively ($P<0.0001$ for EPO 40,000 U QW vs EPO 80,000 U Q3W).

Safety

- Grade 3/4 AEs were observed in 22%, 17%, 22%, and 13% of patients in the EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W groups, respectively ($P>0.56$).
- A total of 7, 7, 5, and 1 patient in the EPO 80,000 U Q3W; EPO 120,000 U Q3W; EPO 40,000 U QW; and DARB 500 µg Q3W groups died while on study, respectively ($P>0.10$). On-study deaths were mostly related to disease progression.

EPO 120,000 U Q3W

Glaspy et al (2009)[3] evaluated the efficacy and safety of EPO at an initial dose of 120,000 U administered Q3W in cancer patients with CT-induced anemia (N=186).

Study Design/Methods

- This was a prospective, randomized, open-label, multicenter study.
- Patients with a non-myeloid malignancy, life expectancy ≥6 months, transferrin saturation >20% and a Hb ≥11.0 g/dL and ≤12.0 g/dL were randomized to either: early

intervention: immediate initiation of EPO 120,000 U SC Q3W (week 1), or standard intervention: initiation of EPO 120,000 U SC Q3W when Hb decreased to <11.0 g/dL.
- Patients who met all other criteria but had a baseline Hb <11.0 g/dL were enrolled into a nonrandomized treatment group.
- If Hb increased to >12.0 g/dL or increased by >1.5 g/dL in a 3-week period during EPO therapy, the dose was reduced as follows: 120,000 U Q3W to 80,000 U Q3W; 80,000 U Q3W to 60,000 U Q3W; or 60,000 U Q3W to 40,000 U Q3W.
- If at any time Hb >13.0 g/dL, EPO was withheld until Hb decreased to <12.0 g/dL, and EPO would be resumed according to the dose reductions previously summarized.
- Hb increases resulting from transfusion administration were not to be used as the basis for EPO dose reduction; however, EPO was always withheld if Hb >13.0 g/dL.
- If Hb decreased by ≥1 g/dL after dose reduction, the previous dose of EPO was reinitiated.
- If Hb <10.0 g/dL after ≥1 dose of EPO, then the patient was considered to have failed treatment with Q3W dosing and was treated with EPO 40,000 U SC QW, starting at that visit.
    - If Hb did not increase by ≥1 g/dL after 4 weeks of therapy at this dose, the EPO dose was increased to 60,000 U SC QW.
    - If Hb did not increase after 4 weeks of treatment with EPO 60,000 U SC QW, the patient was considered to have failed QW dosing.
- EPO was administered for 16 weeks or through the final cycle of CT, whichever came first.
- Patients received ferrous sulfate 325 mg orally once daily, an equivalent oral formulation of iron as tolerated, or an equivalent intravenous formulation.
- **The primary endpoint** was percent value in range, defined as mean proportion of Hb values during CT treatment that were ≥11.0 g/dL and ≤13.0 g/dL.

Results

Patient Characteristics

- Mean baseline Hb was 11.5 g/dL in the early and standard intervention groups and 10.1 g/dL in the nonrandomization group.

Efficacy

- A total of 24%, 33%, and 40% of patients in the early intervention, standard intervention, and nonrandomized groups were nonresponsive to Q3W and switched to QW, respectively.
- A total of 60% (95% confidence interval [CI]: 53%-67%) of patients in the early and standard intervention groups had weekly Hb values during CT in the target range of 11.0-13.0 g/dL.
- Complete success, defined as maintaining all Hb value between 11.0 and 13.0 g/dL during EPO therapy, was achieved by 6% (n=4) patients in the early intervention group.
- In the standard intervention group, 41 patients achieved ≥1 Hb value ≥11.0 g/dL, and 12% (n=5) achieved complete success thereafter.
- Mean Hb values remained between 11.0 and 12.0 g/dL in the randomized groups and between 10.0 and 10.5 g/dL every week in the nonrandomized group.
- Secondary analysis of Hb among patients who did not switch to QW dosing from Q3W revealed significant mean increases in Hb (P<0.05) from baseline for each group: early intervention group: week 3-16 (n=52); standard intervention group: week 11-16 (n=50); nonrandomized group: week 2-16 (n=29).

Safety

- There were 30 drug-related AEs reported, of which 22 were considered possibly related to study drug, 4 were considered probably related to study drug, and 4 (pain, injection site pain, bone pain, and DVT) were considered very likely related to study drug.
- Several AEs, including diarrhea, fatigue, and nausea, were reported in ≥10% of patients in any treatment group; however, these AEs were determined to be consistent with those AEs that have been reported with EPO use in anemic cancer patients receiving myelosuppressive CT.
- Only 1 SAE of pulmonary artery thrombosis in the early intervention group was considered related to study drug.
- A total of 9% (6/68) of patients in the early intervention group, 12% (6/51) of patients in the standard intervention group, and 12% (6/50) of patients in the nonrandomized group experienced ≥1 CRTVE.

Initiation/Maintenance: QW Followed by Q3W

EPO 40,000 U QW Followed by 40,000 U QW or 120,000 U Q3W

Steensma et al (2006)[4] compared maintenance dosing of EPO 120,000 U Q3W and EPO 40,000 U QW in patients with cancer-associated anemia (N=360).

Study Design/Methods

- This was a prospective, 21-week, randomized, multicenter, open-label study that included anemic patients with non-myeloid malignancy believed to be anemic due to active malignancy or antineoplastic therapy.
- Anemia was defined as Hb <12 g/dL for men and Hb <11 g/dL for women.
- All patients were scheduled to receive EPO 40,000 U SC QW for 3 doses (induction phase) and were then randomized to receive for an additional 18 weeks (maintenance phase): EPO 40,000 U SC QW (n=183), or EPO 120,000 U SC Q3W (n=182).
- Dose escalations were not permitted.
- If Hb >13 g/dL, EPO was withheld until Hb ≤12 g/dL, and then EPO was restarted at 30,000 U QW or 80,000 U Q3W, depending on assignment.
- All patients received oral ferrous sulfate 324 mg daily.
- Transfusions were permitted when Hb ≤8.0 g/dL, unless patient was determined to have intolerable ischemic symptoms by the treating physician.
- The primary endpoint was the proportion of patients requiring red blood cell transfusions.

Results

Patient Characteristics

- Overall, 89% were actively receiving CT, and 35% were actively receiving platinum-based CT.

Efficacy

- There was no difference in the proportion of patients requiring transfusions during the study (23% in the 40,000 U QW group and 18% in the 120,000 U Q3W group; *P*=0.22) or specifically during the maintenance phase (13% in the 40,000 U QW group and 15% in the 120,000 U Q3W group; *P*=0.58).
- Mean final Hb±standard deviation was 12.0±1.46 g/dL in the 40,000 U QW group and 11.5±1.50 g/dL in the 120,000 U Q3W group (*P*=0.0006).

Safety

- The incidences of AEs were similar between the 2 treatment groups.

- EPO doses were more frequently withheld in the 40,000 U QW group compared with the 120,000 U Q3W group for Hb levels >13.0 g/dL (61% vs 36%, respectively; *P*<0.0001).
- Incidence of ischemic or thrombotic events of any type was comparable between groups: n=8 in the 40,000 U QW group and n=9 in the 120,000 U Q3W group (*P*=0.80).
- During the treatment phase, 27 (8%) patients died, of which 14 patients were in the 40,000 U QW group and 13 patients were in the 120,000 U Q3W group.
- Median survival time: 377 days (79 deaths) in the 40,000 U QW group and 403 days (73 deaths) in the 120,000 U Q3W group.

EPO 60,000 U QW Followed by 80,000 U Q3W

Montoya et al (2007)[5] evaluated the safety and efficacy of EPO at a starting dose of 60,000 U QW followed by maintenance doses of 80,000 U Q3W in patients with CT-induced anemia (N=115).

Study Design/Methods

- This was a prospective, open-label, single-arm, multicenter study that included patients with non-myeloid malignancy, Hb ≤11 g/dL, and scheduled to receive CT Q3W.
- There were 2 treatment phases: an IDP when EPO was administered as 60,000 U SC QW for up to 12 weeks until a target Hb of 12 g/dL was achieved and an extended dosing phase (EDP) when EPO was administered as 80,000 U SC Q3W at the beginning of the next CT cycle.
- Patients were withdrawn from the study if they did not achieve a Hb of 12 g/dL in the IDP or if Hb decreased <11 g/dL in the EDP.
- For either phase, EPO was withheld if Hb >13 g/dL and was resumed at a reduced dose (40,000 U SC QW during the IDP and 60,000 SC Q3W during the EDP) when Hb decreased to ≤12 g/dL. The dose was reduced similarly if Hb increased >1.3 g/dL in any 2-week period.
- Oral ferrous sulfate 325 mg was administered to all patients as needed and as tolerated.
- The maximum study duration was 24 weeks for both phases.
- **The primary efficacy endpoint** was the proportion of patients achieving hematopoietic response, defined as Hb increase from baseline ≥2 g/dL or Hb ≥12 g/dL during IDP.

Results

Patient Characteristics

- Mean baseline Hb was 10.2±0.84 g/dL.

Efficacy

- In the IDP, among evaluable patients, hematopoietic response was achieved in 76.4% (84/110) of patients.
  - A total of 5.5% of patients achieved a ≥1.0 to ≤1.9 g/dL rise in Hb from baseline.
  - A total of 17/115 patients received blood transfusions.
- The mean Hb level at start of the EDP was 12.3±0.62 g/dL and the mean Hb level during this phase was 12.0±0.72 g/dL.
  - A total of 87.7% of patients maintained average Hb between >11.0 g/dL and ≤13.0 g/dL and 74.0% maintained average Hb between >11.0 g/dL and ≤12.5 g/dL.
  - A total of 2/73 patients received blood transfusions.

Safety

- The most commonly reported AEs included: nausea (38.3%), fatigue (32.2%), neutropenia (25.2%), vomiting (22.6%), and diarrhea (20.9%).
- Grade 3 and grade 3/4 neutropenia were reported in 6 and 13 patients, respectively.
- SAEs were reported in 44.3% (n=51) of patients; the most commonly SAEs reported included: dehydration (7%), febrile neutropenia (6.1%), and pyrexia (6.1%).

- CRTVEs were experienced by 7.8% (n=9) of patients in the IDP and none during the EDP; none of the thrombotic vascular events were considered related to study drug.

LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 03 September 2024. To streamline this document and provide the most relevant and timely information, only prospective studies with >50 patients are summarized above. Smaller prospective studies (N≤50) and retrospective analyses are cited in the Summary section.

REFERENCES

1. PROCRIT (epoetin alfa) [Prescribing Information]. Horsham, PA: Janssen Products, LP;https://imedicalknowledge.veevavault.com/ui/approved_viewer?token=7994-2b94d073-29d7-4d37-b818-d662fd16ca16.

2. Steensma DP, Dakhil SR, Novotny PJ, et al. A randomized comparison of once weekly epoetin alfa to extended schedule epoetin or darbepoetin in chemotherapy-associated anemia. *Am J Hematol*. 2015;90(10):877-881.

3. Glaspy JA, Charu V, Luo D, et al. Initiation of epoetin-alpha therapy at a starting dose of 120,000 units once every 3 weeks in patients with cancer receiving chemotherapy: an open-label, multicenter study with randomized and nonrandomized treatment arms. *Cancer*. 2009;115(5):1121-1131.

4. Steensma DP, Molina R, Sloan JA, et al. Phase III study of two different dosing schedules of erythropoietin in anemic patients with cancer. *J Clin Oncol*. 2006;24(7):1079-1089.

5. Montoya VP, Xie J, Williams D, et al. An extended maintenance dosing regimen of epoetin alfa 80,000 U every 3 weeks in anemic patients with cancer receiving chemotherapy. *Support Care Cancer*. 2007;15(12):1385-1392.

6. Patton J, Kuzur M, Liggett W, et al. Epoetin alfa 60,000 U once weekly followed by 120,000 U every 3 weeks increases and maintains hemoglobin levels in anemic cancer patients undergoing chemotherapy. *Oncologist*. 2004;9(1):90-96.

7. Chang J, Phippard L, Sharma D, et al. A phase II randomized trial of three loading doses of epoetin alfa followed by every three-week (q3w) dosing in cancer patients receiving chemotherapy. *J Clin Oncol*. 2005;23(16, Suppl):8219-8219.

8. Burton T, Larholt K, Peake C, et al. Erythropoiesis-stimulating agents in cancer patients receiving chemotherapy: Real-world dosing, hematologic outcomes, and costs. Poster presented at: American College of Clinical Pharmacy (ACCP) 2007 Annual Meeting; October 14-17, 2007; Denver, CO.

9. Barron J, Mody S, Boudreaux M, et al. Dosing distribution patterns and associated costs of erythropoietic agents in anemic patients with cancer receiving chemotherapy. Poster presented at: The 40th American Society of Health-System Pharmacists (ASHP) Midyear Clinical Meeting and Exhibition; December 4-8, 2005; Las Vegas, NV.

10. Gosselin A, Lafeuille M, Bookhardt B, et al. Drug utilization and cost considerations of erthropoiesis-stimulating agents (ESAs) in a managed care cancer population receiving chemotherapy. Poster presented at: International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 13th Annual International Meeting; May 3-7, 2008; Toronto, ON, Canada.

11. Gosselin A, Lafeuille M, Bookhart B, et al. Drug utilization patterns and cost for erythropoiesis-stimulating agents in patients with breast, lung, or gastrointestinal cancer receiving chemotherapy. Poster presented at: The American College of Clinical Pharmacy (ACCP) Annual Meeting; October 19-22, 2008; Louisville, KY.

12. Harley C, Muser E, Nelson M, et al. Epoetin alfa and darbepoetin alfa utilization patterns among cancer patients. Poster presented at: The 40th American Society of Health-System Pharmacists (ASHP) Midyear Clinical Meeting and Exhibition; December 4-8, 2005; Las Vegas, NV.

13. Harris H, del A, M, et al. Anemia treatment costs in cancer patients treated with epoetin alfa or darbepoetin alfa in a managed-care population. Poster presented at: The Academy of Managed Care Pharmacy (AMCP); October 5-8, 2005; Nashville, TN.

14. Laliberté F, McKenzie R, Vekeman F, et al. Drug utilization and cost considerations of erythropoiesis-stimulating agents in cancer patients receiving chemotherapy: results from a large managed-care database. Poster presented at: Academy of Managed Care Pharmacy 21st Annual Meeting; April 15-18, 2009; Orlando, FL.

15. Lefebvre P, Gosselin A, McKenzie RS, et al. Dosing patterns, treatment costs, and frequency of physician visits in adults with cancer receiving erythropoietic agents in managed care organizations. *Curr Med Res Opin*. 2006;22(9):1623-1631.

16. Mark TL, McKenzie RS, Fastenau J, et al. Retrospective observational study of patients with chemotherapy-related anemia receiving erythropoietic agents. *Curr Med Res Opin*. 2005;21(9):1347-1354.

17. McLaughlin T, Mody S, McKenzie R. Real-world dosing of erythropoietic agents in a nationwide sample of patients with cancer receiving chemotherapy: results from a large retrospective, observational study. Poster presented at: The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 11th Annual International Meeting; May 20-24, 2006; Philadelphia, PA.

18. Vekeman F, McKenzie RS, Bookhart BK, et al. Drug utilisation and cost considerations of erythropoiesis stimulating agents in oncology patients receiving chemotherapy: observations from a large managed-care database. *J Med Econ*. 2009;12(1):1-8.

19. Muller RJ, Baribeault D. Extended-dosage-interval regimens of erythropoietic agents in chemotherapy-induced anemia. *Am J Health Syst Pharm*. 2007;64(24):2547-2556.